



# ***Role of Chitosan Nanoparticle and Low Doses of Gamma Irradiation in Reducing Induced Pancreatitis***

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*I declare that this thesis has been composed by me and it has not been submitted for a degree at this or any other university.*

**MAHITAB IBRAHIM KHALIL**

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# Abstract

L-arginine (ARG) induced acute pancreatitis was evaluated as a novel and distinct form of experimental pancreatitis. Chitosan nanospheres have gained more attention as drug. The strategy of the study was carried out to evaluate the curative anti-pancreatitis effect of chitosan nanoparticles (ChNPs) (0.5 mg/kg/day for 15 days) and exposure to 1 Gy whole body gamma irradiation as a fractionated dose (0.25Gy up to 1 Gy) in rats treated with repeated doses of ARG (250 mg/ rat twice at one hour interval, day other day for 10 days). Male albino rats were divided into 8 groups, all animals were sacrificed after 1 and 14 days post treatments.

Pancreatic cells damage and the anti-pancreatitis effect were evaluated by biochemical and histopathological studies which revealed that arginine caused an increase in amylase, lipase and LDH activities, as well as NO, MDA levels, while a decrease in antioxidant SOD activity was recorded besides the observed increase in inflammatory cytokines IL-1 $\beta$  and TNF- $\alpha$ , as well as, the increase in Urea, cholesterol, triglycerides and LDL-C levels, while a decrease in HDL-C level was noticed.

ChNPs and low doses of  $\gamma$ - irradiation (individually or combined) represented a very good deal of amelioration in the

levels of biochemical markers previously mentioned, moreover the histological investigations confirmed the biochemical results.

# LIST OF ABBREVIATIONS

A	Absorbance
AIDS	Acquired immune deficiency disease
AP	Acute Pancreatitis
ARG	L-Arginine
ASL	argininosuccinate lyase
ASS	argininosuccinate synthetase
b.Wt.	Body weight
BUN	Blood Urea Nitrogen
CAT	catalase
CDNB	1-chloro-2,4-dinitrobenzene
CEH	cholesterol esterase
ChNPs	Chitosan Nano Particles
CHOD	cholesterol oxidase
CIA	Collagen-induced Arthritis
cNOS	constitutive NO synthase
CNP	2-chloro-4-nitrophenol
CNS	Central nervous system
Conc.	Concentration
CP	Chronic pancreatitis
DD	Degree of Deacetylation
DGMRE	Lipase substrate 3-glutaric acid-(6-methyl-resorufin)-ester
DNPH	dinitrophenyl hydrazine
DPN	Diphenyl amine
DSBs	double-strand breaks
EAE	experimental encephalomyelitis
EDTA	Ethylene diamine tetra-acetic acid
FDA	Food and Drug Administration
GALG2-CNP	2-chloro-4-nitrophenyl-1-galactopyranosyl-

	maltoside
GK	Glycerokinase
GRAS	Generally Recognized as Safe
GS	Glutathione synthase
GSH	Reduced glutathione
GSH-PX	glutathione peroxidase
GSSG	Oxidized glutathione
GST	Glutathione-S-transferase
Gy	Gray (unit of radiation)
H <sup>+</sup>	Proton
HC	Hyperchromatisation
HCL	Hydrochloric acid
HDL-C	High density lipoprotein- cholesterol
HIV	Human Immunodeficiency Virus
HMG-COA	3 Hydroxy-methyl glutaryl coenzyme
HO-1	heme oxygenase 1
H <sub>2</sub> O <sub>2</sub>	Hydrogen peroxide
IFN- $\gamma$	interferon gamma
IFN- $\gamma$	interferon- $\gamma$
IL-1	interleukin-1
IL-10	Interleukin -10
IL-1 $\beta$	Interleukin 1 beta.
IL-4	Interleukin -4
IL-6	Interleukin -6
IL-8	Interleukin -8
iNOS	Inducible nitric oxide synthase
iNOS	inducible NO synthase
I.P	Intraperitoneal
IR	Irradiated group
KH <sub>2</sub> PO <sub>4</sub>	potassium dihydrogen phosphate
LD <sub>50</sub>	Lethal Dose 50
LDH	Lactate dehydrogenase
LDH	Lactate dehydrogenase
LDL	Low density lipoprotein

LDL-C	Low density lipoprotein- cholesterol
LD-RT	low-dose radiotherapy
LP	Lipid peroxidation
MDA	Malondialdehyde
MMPs	matrix metalloproteinases
M.W	Molecular Weight
Na <sub>2</sub> HPO <sub>4</sub>	anhydrous disodium hydrogen phosphate
NAD	Nicotinamide adenine dinucleotide
NADH	Nicotinamide adenine dinucleotide (reduced form)
NADPH	Nicotinamide adenine dinucleotide phosphate
NaOH	Sodium Hydroxide
NBT	nitroblue tetrazolium
NCRRT	National Center for Radiation research and Technology
NEDD	N-1-naphthyl ethylenediamine dihydrochloride
NF-κB	Nuclear factor –kappa B
NIH	US National Institute of Health
NO	Nitric oxide
NOS	NO synthase
NO <sub>x</sub>	nitrite /nitrate
O <sub>2</sub>	Oxygen molecule
O <sub>2</sub> <sup>•-</sup>	Superoxide
O.D.	Optical density
OH <sup>•</sup>	Hydroxyl radical
ONOO <sup>-</sup>	Peroxynitrite
PDGF	Platelet-derived growth factor
POD	peroxidase
RNA	Ribonucleic acid
RNS	Reactive Nitrogen Species
ROO <sup>-</sup>	lipid peroxides
ROS	Reactive oxygen species
r.p.m	Rotation per minute
-SH	Sulfhydryl group
SIRS	systemic inflammatory response

	syndrome
SOD	Superoxide dismutase
SSBs	Single strand breaks
TBA	Thiobarbituric acid
TCA	Trichloroacetic acid
TGF-beta	Tumor Growth Factor beta
TNF- $\alpha$	Tumor necrosis factor alpha
TQ10	Total Q10
VCL <sub>3</sub>	Vanadium trichloride
VLDL	Very low density lipoproteins

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